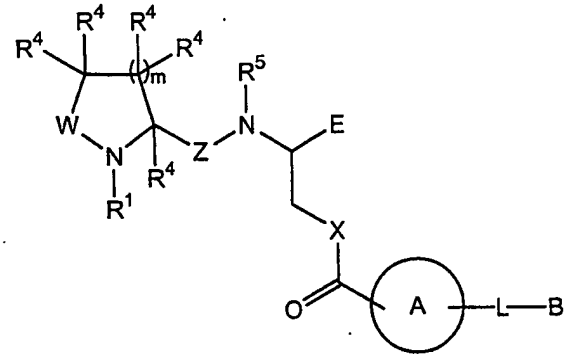
CLAIMS

1.- A compound of general formula I:



I

wherein:

R^1 represents $-SO_2R^2$, $-COR^2$ or $-CH_2R^3$;

R^2 represents C_{1-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, which can be optionally substituted with one or more groups R^a, or R^2 represents Cy, CyC_{1-4} alkyl, CyC_{2-4} alkenyl or CyC_{2-4} alkynyl, where the groups Cy can be optionally substituted with one or more groups R^b;

R^3 represents hydrogen, C_{1-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, where the groups C_{1-8} alkyl, C_{2-8} alkenyl and C_{2-8} alkynyl can be optionally substituted with one or more groups R^c, or R^3 represents Cy or CyC_{1-4} alkyl, where the groups Cy can be optionally substituted with one or more groups selected from R^c and R^d;

each R^4 independently represents hydrogen, C_{1-8} alkyl, Cy or CyC_{1-4} alkyl, where the C_{1-8} alkyl group can be optionally substituted with one or more groups R^c and where the groups Cy can be optionally substituted with one or more groups selected from R^c and R^d;

W represents $-CR^4R^4-$ when R^1 is $-SO_2R^2$ or $-COR^2$, or W represents -CO- when R^1 is $-CH_2R^3$;

Z represents -CO- or -CS-;

E represents $-COOR^6$, $-CONR^7R^8$ or 5-tetrazolyl;

X represents $-CH_2-$, $-NR^5-$ or -O-;

each R^5 independently represents hydrogen or C_{1-4} alkyl;

R^6 represents hydrogen, C_{1-8} alkyl, C_{3-7} cycloalkyl or aryl, where the C_{1-8} alkyl group can be optionally substituted with a group selected from C_{3-7} cycloalkyl, aryl, $-OR^g$, $-OCOR^d$, $-OCOOR^d$, $-COOR^g$ and $-NHCOR^g$ and the aryl

groups can be optionally substituted with one or more groups R^b;

R^7 represents hydrogen, C_{1-8} alkyl, C_{3-7} cycloalkyl, aryl or $-SO_2R^d$, where the C_{1-8} alkyl group can be optionally substituted with a group selected from C_{3-7} cycloalkyl, aryl, $-SO_2R^d$, $-COOR^g$ and $-COR^d$;

R^8 represents hydrogen or C_{1-8} alkyl;

or R^7 and R^8 together with the nitrogen atom to which they are bound can form a cycle Het^1;

A represents C_{3-7} cycloalkyl or Het^1, which can be optionally substituted with one or more groups selected from oxo, C_{1-8} alkyl and C_{1-8} haloalkyl;

L represents $-(CR^9R^9)_n-$;

each R^9 independently represents hydrogen or C_{1-4} alkyl;

B represents:

i) C_{3-7} cycloalkyl, Het^1 or Het^2, which can be optionally substituted with one or more groups selected from oxo, R^b and Cy optionally substituted with one or more groups R^b; or

ii) a group selected from $-COR^e$, $-NR^fR^f$, $-OR^f$, $-SR^f$, $-S(O)_pR^e$, $-CONR^fR^f$, $-NR^fCOR^f$, $-NR^fCONR^fR^f$, $-NR^fCSNR^fR^f$, $-NR^fCOOR^e$, $-OCOR^e$, $-OCONR^fR^f$, $-NR^fSO_2R^e$ and $-SO_2NR^fR^f$;

m represents 0 or 1;

n represents 1, 2, 3 or 4;

p represents 1 or 2;

each R^a independently represents halogen, $-COR^d$, $-OR^g$, $-NR^gR^g$, $-COOR^g$, $-OCOR^d$, $-CONR^gR^g$, $-NR^gCOR^g$, $-OCONR^gR^g$ or $-NR^gCOOR^d$;

each R^b independently represents a group R^a, $-NO_2$, $-SR^g$, $-S(O)_pR^d$ or C_{1-8} alkyl optionally substituted with one or more groups R^c;

each R^c independently represents halogen, $-OR^h$ or $-NR^hR^h$;

each R^d independently represents C_{1-8} alkyl, C_{3-7} cycloalkyl or aryl, which can be optionally substituted with one or more groups R^c;

each R^e independently represents C_{1-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, which can be optionally substituted with one or more groups R^a, or R^e represents Cy or CyC_{1-4} alkyl, where the groups Cy can be optionally substituted with one or more groups selected from oxo, Cy* and R^b, and where the groups Cy* can be optionally substituted with one or more groups selected from oxo and R^b;

each R^f independently represents hydrogen or any of the meanings

described for R^e;

or two groups R^f placed on the same nitrogen atom can be attached to each other to form together with said nitrogen atom a cycle Het^1 which can be optionally substituted with one or more groups selected from oxo, Cy and R^b, where the groups Cy can be optionally substituted with one or more groups selected from oxo and R^b;

each R^g independently represents hydrogen or any of the meanings described for R^d;

or two groups R^g placed on the same nitrogen atom can be attached to each other to form together with said nitrogen atom a cycle Het^1 which can be optionally substituted with one or more groups selected from oxo, Cy and R^b, where the groups Cy can be optionally substituted with one or more groups selected from oxo and R^b;

each R^h independently represents hydrogen, C_{1-8} alkyl, C_{3-7} cycloalkyl or aryl, where the groups C_{1-8} alkyl, C_{3-7} cycloalkyl and aryl can be optionally substituted with one or more halogen atoms;

Cy and Cy* independently represent aryl, C_{3-7} cycloalkyl, Het^1 or Het^2;

aryl in the above definitions represents phenyl or naphthyl;

Het^1 in the above definitions represents a saturated or insaturated non-aromatic 5- to 7-membered monocyclic ring containing from one to four heteroatoms selected from N, O and S, which can be optionally fused to a phenyl, naphthyl or Het^2 ring, and which is chemically stable and obtainable through chemical synthesis; and

Het^2 in the above definitions represents an aromatic 5- to 7-membered monocyclic or 9- to 11-membered bicyclic ring, which contains from one to four heteroatoms selected from N, O and S, and which is chemically stable and obtainable through chemical synthesis;

and the salts, solvates and prodrugs thereof.

2.- A compound according to claim 1 wherein R^1 represents $-SO_2R^2$.

3.- A compound according to claim 1 or 2 wherein R^2 represents aryl optionally substituted with one or more groups R^b.

4.- A compound according to any of claims 1 to 3 wherein all the groups R^4 represent hydrogen.

5.- A compound according to any of claims 1 to 4 wherein R^5 represents

hydrogen.

6.- A compound according to any of claims 1 to 5 wherein W represents $-CR^4R^4-$.

7.- A compound according to claim 6 wherein W represents $-CH_2-$.

8.- A compound according to any of claims 1 to 7 wherein Z represents -CO-.

9.- A compound according to any of claims 1 to 8 wherein E represents $-COOR^6$.

10.- A compound according to claim 9 wherein E represents -COOH.

11.- A compound according to any of claims 1 to 10 wherein m represents 1.

12.- A compound according to any of claims 1 to 11 wherein X represents -NH-.

13.- A compound according to any of claims 1 to 11 wherein X represents $-CH_2-$.

14.- A compound according to any of claims 1 to 11 wherein X represents -O-.

15.- A compound according to any of claims 1 to 14 wherein A represents piperidine or piperazine.

16.- A compound according to any of claims 1 to 15 wherein L represents $-(CH_2)_n-$.

17.- A compound according to claim 16 wherein L represents methylene or ethylene.

18.- A compound according to any of claims 1 to 17 wherein B represents Het^1 or Het^2 optionally substituted with one or more groups selected from oxo, R^b and Cy optionally substituted with one or more groups R^b.

19.- A compound according to claim 18 wherein B represents imidazopyridine optionally substituted with one or more groups selected from oxo, R^b and Cy optionally substituted with one or more groups R^b.

20.- A compound according to any of claims 1 to 17 wherein B represents $-NR^fR^f$, $-OR^f$, $-NR^fCOR^f$, $-NR^fCONR^fR^f$, $-NR^fCSNR^fR^f$, $-NR^fCOOR^e$ or $-OCONR^fR^f$.

21.- A compound according to claim 20 wherein B represents $-OCONR^fR^f$.

22.- A compound according to claim 21 wherein both groups R^f are attached to each other to form together with the nitrogen atom a cycle Het^1, which can be optionally substituted with one or more groups selected from oxo, Cy and R^b, wherein the groups Cy can be optionally substituted with one or more groups selected from oxo and R^b.

23.- A compound according to claim 1 selected from:

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-oxooxazolidin-3-ylmethyl)piperidin-1-yl]pentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-oxopyrrolidin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-oxoisoindolin-2-ylmethyl)piperidin-1-yl]pentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-ethyl-5,7-dimethylimidazo[4,5-*b*]pyridin-3-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl (*2S*)-5-[4-(2-methylimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoate;

methyl (*2S*)-5-oxo-5-[4-[(2-oxopyrrolidin-1-yl)methyl]piperidin-1-yl]-2-[1-tosyl-L-prolylamino]pentanoate;

methyl (*2S*)-5-oxo-5-[4-(2-phenylimidazol-1-ylmethyl)piperidin-1-yl]-2-[1-tosyl-L-prolylamino]pentanoate;

methyl (*2S*)-5-[4-[[1-(2-ethoxyethyl)benzimidazol-2-yl]methyl]piperazin-1-yl]-5-oxo-2-[[1-tosyl-L-prolyl]amino]pentanoate;

methyl (*2S*)-5-oxo-5-[4-(2-pyridylmethyl)piperazin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoate;

methyl (*2S*)-5-oxo-5-[4-(1-oxoisoindolin-2-ylmethyl)piperidin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoate;

methyl (*2S*)-5-oxo-5-[4-(2-thienylmethyl)piperazin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoate;

methyl (*2S*)-5-[4-[(2,5-dioxopyrrolidin-1-yl)methyl]piperidin-1-yl]-5-oxo-2-[[1-tosyl-L-prolyl]amino]pentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(3-methylbutanoylamino)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (*2S*)-5-[4-[(*N'-tert*-butylureido)methyl]piperidin-1-yl]-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxopentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(isobutoxycarbonylamino)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (*2S*)-5-oxo-2-[1-tosyl-L-prolyl]amino-5-[4-[[4-(trifluoromethyl)pyrimidin-2-yl]aminomethyl]piperidin-1-yl]pentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(isopropylsulfonylamino)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (*2S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(*N'*-isopropylthioureido)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(2-ethyl-5,7-dimethylimidazo[4,5-*b*]pyridin-3-yl)ethyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(pyrrolidin-1-ylcarbonyloxy)ethyl]piperidin-1-yl]pentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(4-methylpiperazin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(4-morpholinyl)ethyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[[(dimethylaminoacetyl)amino]methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(diethylamino)ethyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(1-pyrrolidinyl)ethyl]piperidin-1-yl]pentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-[(2-methoxyethyl)aminocarbonyloxy]ethyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(4-morpholinylcarbonylaminomethyl)piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-pyrrolidinylcarbonylaminomethyl)piperidin-1-yl]pentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-piperidylmethyl)piperidin-1-yl]pentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[[*N*-ethyl-*N*-(trifluoroacetyl)amino]methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[[(4-methylpiperazin-1-yl)carbonylamino]methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(4-pyridylaminomethyl)piperidin-1-yl]pentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(*N*-ethyl-*N*-isobutoxycarbonylamino)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl (2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-methylimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-pyrrolylmethyl)piperidin-1-yl]pentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2,5-dimethylpyrrol-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(dimethylaminomethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(dimethylamino)ethyl]piperazin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-ethylimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-oxo-2,3-dihydroimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]pentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-isopropylaminoimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(diethylaminomethyl)piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(2-methylimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(dimethylaminomethyl)piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-3-[[4-(1-piperidylmethyl)piperidin-1-ylcarbonyl]amino]-2-[*N*-tosyl-L-prolyl]aminopropionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[4-(dimethylaminomethyl)piperidin-1-ylcarbonyloxy]propionate;

methyl *(2S)*-5-[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-5-[4-[(diethylaminocarbonyloxy)methyl]piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(4-methylpiperazin-1-yl)carbonyloxymethyl]piperidin-1-yl]-5-oxopentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(4-pyridyloxymethyl)piperidin-1-yl]pentanoate;

methyl *(2S)*-5-[4-(4-methylpiperazin-1-ylmethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoate;

methyl (2*S*)-5-[4-(dimethylaminomethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoate;

(2*S*)-5-[4-[(1-oxoisoindolin-2-yl)methyl]piperidin-1-yl]-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(3-methylbutanoylamino)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-5-[4-[(*N'-tert*-butylureido)methyl]piperidin-1-yl]-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(isobutoxycarbonylamino)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(*N'*-isopropylthioureido)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(2-ethyl-5,7-dimethylimidazo[4,5-*b*]pyridin-3-yl)ethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(isopropylsulfonylamino)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(pyrrolidin-1-ylcarbonyloxy)ethyl]piperidin-1-yl]pentanoic acid;

(2*S*)-5-oxo-5-[4-[(2-oxopyrrolidin-1-yl)methyl]piperidin-1-yl]-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2*S*)-5-oxo-5-[4-(2-phenylimidazol-1-ylmethyl)piperidin-1-yl]-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2*S*)-5-oxo-2-[1-tosyl-L-prolyl]amino-5-[4-[[4-(trifluoromethyl)pyrimidin-2-yl]aminomethyl]piperidin-1-yl]pentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-ethyl-5,7-dimethylimidazo[4,5-*b*]pyridin-3-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-[(2-methoxyethyl)aminocarbonyloxy]ethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(4-morpholinylcarbonylaminomethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-pyrrolidinylcarbonylaminomethyl)piperidin-1-yl]pentanoic acid;

(2*S*)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-5-[4-[(diethylaminocarbonyloxy)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-oxooxazolidin-3-ylmethyl)piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-oxopyrrolidin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-methylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-5-[4-(2-methylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2S)-5-[4-[[1-(2-ethoxyethyl)benzimidazol-2-yl]methyl]piperazin-1-yl]-5-oxo-2-[[1-tosyl-L-prolyl]amino]pentanoic acid;

(2S)-5-oxo-5-[4-(2-pyridylmethyl)piperazin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoic acid;

(2S)-5-oxo-5-[4-(1-oxoisoindolin-2-ylmethyl)piperidin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoic acid;

(2S)-5-oxo-5-[4-(2-thienylmethyl)piperazin-1-yl]-2-[[1-tosyl-L-prolyl]amino]pentanoic acid;

(2S)-5-[4-[(3-carboxypropionylamino)methyl]piperidin-1-yl]-5-oxo-2-[[1-tosyl-L-prolyl]amino]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(4-methylpiperazin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(4-morpholinyl)ethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-pyrrolylmethyl)piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2,5-dimethylpyrrol-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(dimethylaminomethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(dimethylamino)ethyl]piperazin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-ethylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-oxo-2,3-dihydroimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(2-isopropylaminoimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-(diethylaminomethyl)piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(2-methylimidazo[4,5-*c*]pyridin-1-ylmethyl)piperidin-1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[[(dimethylaminoacetyl)amino]methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-(diethylamino)ethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(1-pyrrolidinyl)ethyl]piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(1-piperidylmethyl)piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(dimethylaminomethyl)piperidin-1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(ethylamino)methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[[(4-methylpiperazin-1-yl)carbonylamino]methyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[4-(dimethylaminomethyl)piperidin-1-ylcarbonyloxy]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(4-pyridylaminomethyl)piperidin-1-yl]pentanoic acid;

(2S)-5-[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(4-methylpiperazin-1-yl)carbonyloxymethyl]piperidin-1-yl]-5-oxopentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(4-pyridyloxymethyl)piperidin-1-yl]pentanoic acid;

(2S)-5-[4-(4-methylpiperazin-1-ylmethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2S)-5-[4-(dimethylaminomethyl)piperidin-1-yl]-5-oxo-2-[1-tosyl-L-prolylamino]pentanoic acid;

(2S)-3-[[4-(1-piperidylmethyl)piperidin-1-ylcarbonyl]amino]-2-[*N*-tosyl-L-prolyl]aminopropionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-[4-[(*N*-ethyl-*N*-isobutoxycarbonylamino)methyl]piperidin-1-yl]-5-oxopentanoic acid;

methyl (2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(4-methylpiperidin-1-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[[4-(ethoxycarbonyl)piperazin-1-yl]carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[[4-(4-pyridyl)piperazin-1-yl]carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(cis-2,6-dimethylmorpholin-4-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionate;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(4-methylhomopiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionic acid;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(2-ethylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-ylcarbonyl]amino]propionate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(4-phenylpiperazin-1-ylcarbonyloxy)ethyl]piperidin-1-yl]pentanoate;

methyl *(2S)*-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-propylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]pentanoate;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(4-methylpiperazin-1-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-[2-(4-phenylpiperazin-1-ylcarbonyloxy)ethyl]piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(4-methylpiperidin-1-yl)carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolylamino]-5-oxo-5-[4-(2-propylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-yl]pentanoic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[[4-(ethoxycarbonyl)piperazin-1-yl]carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[[4-(4-pyridyl)piperazin-1-yl]carbonyloxy]ethyl]piperidin-1-ylcarbonyl]amino]propionic acid;

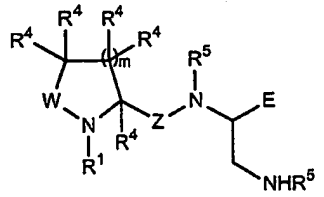
(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-[2-[(cis-2,6-dimethylmorpholin-4-yl)carbonyloxy]ethyl]piperidin -1-ylcarbonyl]amino]propionic acid;

(2S)-2-[1-(3,5-dichlorophenylsulfonyl)-L-prolyl]amino-3-[[4-(2-ethylimidazo[4,5-c]pyridin-1-ylmethyl)piperidin-1-ylcarbonyl]amino]propionic acid;

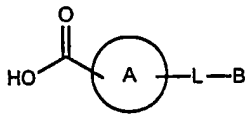
or a salt, solvate or prodrug thereof.

24.- A process for preparing a compound of formula I according to claim 1, which comprises:

(a) when in a compound of formula I X represents -NR^5-, reacting an amine of formula II with an acid of formula III



II

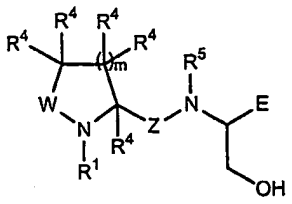


III

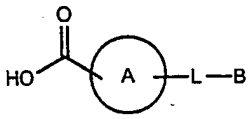
wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1;

or

(b) when in a compound of formula I X represents -O-, reacting an alcohol of formula IV with an acid of formula III



IV

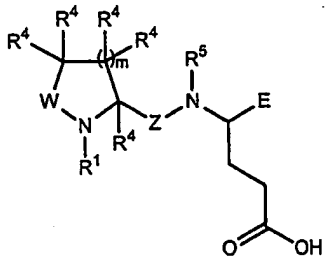


III

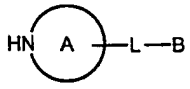
wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1;

or

(c) when in a compound of formula I X represents $-CH_2-$ and cycle A is bound to the carbonyl group through a nitrogen atom, reacting an acid of formula V with an amine of formula VI



V

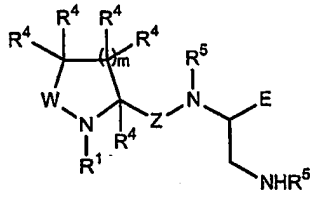


VI

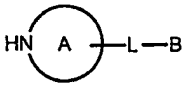
wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1;

or

(d) when in a compound of formula I X represents $-NR^5-$ and cycle A is bound to the carbonyl group through a nitrogen atom, reacting an amine of formula II previously activated with an activating agent suitable for the preparation of ureas with an amine of formula VI

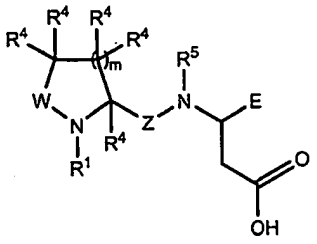


II

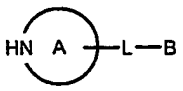


VI

wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1, or reacting an amine of formula VI previously activated with an activating agent suitable for the preparation of ureas with an amine of formula II, or alternatively reacting a compound of formula V' previously activated with an azide suitable for a Curtius rearrangement with an amine of formula VI



V'

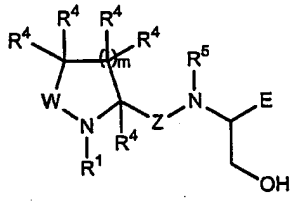


VI

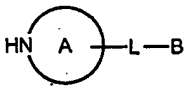
wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1;

or

(e) when in a compound of formula I X represents -O- and cycle A is bound to the carbonyl group through a nitrogen atom, reacting an alcohol of formula **IV** previously activated with an activating agent suitable for the preparation of carbamates with an amine of formula **VI**



IV

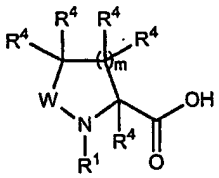


VI

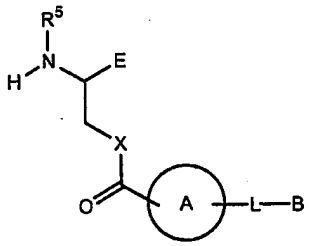
wherein R^1, R^4, R^5, W, Z, E, A, L, B and m have the meaning described in claim 1;

or

(f) when in a compound of formula I Z represents -CO-, reacting an acid of formula **VII** with an amine of formula **XVII**



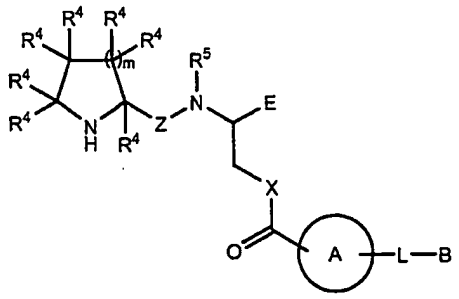
VII



XVII

wherein R^1, R^4, R^5, W, E, X, A, L, B and m have the meaning described above; or

(g) when in a compound of formula I W represents $-CR^4R^4-$ and R^1 represents $-SO_2R^2$, reacting a compound of formula **XVIII** with a sulfonyl chloride of formula **IX**



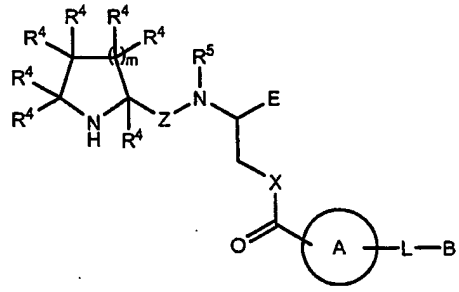
$ClSO_2R^2$

XVIII **IX**

wherein R^2, R^4, R^5, Z, E, X, A, L, B and m have the meaning described in claim 1;

or

(h) when in a compound of formula I W represents $-CR^4R^4-$ and R^1 represents $-COR^2$, reacting a compound of formula **XVIII** with an acid of formula **X**



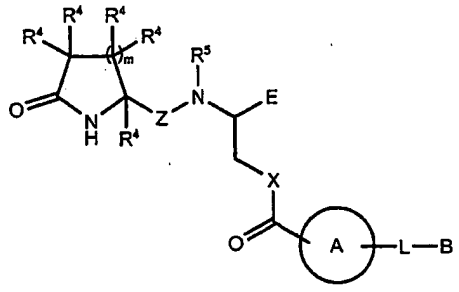
R^2COOH

XVIII **X**

wherein R^2, R^4, R^5, Z, E, X, A, L, B and m have the meaning described in claim 1;

or

(i) when in a compound of formula I W represents -CO- and R^1 represents $-CH_2R^3$, reacting a compound of formula **XIX** with a compound of formula **XI**



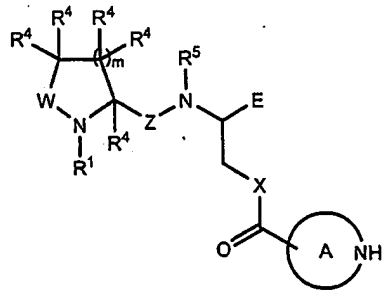
R^3-CH_2-D

XIX **XI**

wherein R^2, R^4, R^5, Z, E, X, A, L, B and m have the meaning described in claim 1 and D represents a good leaving group; or

(j) when in a compound of formula I cycle A is bound to the -L-B moiety through a ring nitrogen atom, alkylating the secondary amine of a compound of formula **XX**

with a compound of formula XIV



D-L-B

XX XIV

wherein R^1, R^4, R^5, W, Z, E, X, A, L, B and m have the meaning described in claim 1 and D represents a good leaving group; or

(k) transforming, in one or a plurality of steps, a compound of formula I into another compound of formula I; and

(l) if desired, after the above steps, reacting a compound of formula I with an acid or a base to give the corresponding addition salt.

25.- A pharmaceutical composition which comprises an effective amount of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof and one or more pharmaceutically acceptable excipients.

26.- Use of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof for the manufacture of a medicament for the treatment or prevention of diseases mediated by integrins α_4.

27.- Use according to claim 26 wherein the disease mediated by integrins α_4 is selected from inflammatory diseases, immune diseases, autoimmune diseases, degenerative disorders, tumor metastasis and ischemia-reperfusion disorders.

28.- Use of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof for the manufacture of a medicament for the treatment or prevention of inflammatory, immune and/or autoimmune diseases.

29.- Use according to claim 28 wherein the inflammatory, immune and/or autoimmune disease is selected from diseases with an allergic component, inflammatory diseases with an autoimmune component, inflammatory bowel disease, inflammatory processes having an alloimmune origin caused by

transplants or rejections, inflammatory processes that develop as a consequence of blood vessel revascularization treatments, encephalomyelitis, hepatitis, bronchitis, vasculitis and atherosclerosis.

30.- Use according to claim 29 wherein the disease with an allergic component is selected from asthma, allergic rhinitis, allergic dermatitis and allergic conjunctivitis.

31.- Use according to claim 29 wherein the inflammatory disease with an autoimmune component is selected from rheumatoid arthritis, psoriatic arthritis, multiple sclerosis, psoriasis and diabetes.

32.- Use according to claim 29 wherein the inflammatory bowel disease is selected from Crohn's disease and ulcerative colitis.

33.- Use of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof for the manufacture of a medicament for the treatment or prevention of degenerative disorders.

34.- Use according to claim 33 wherein the degenerative disorder is selected from Alzheimer's disease and arthrosis.

35.- Use of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof for the manufacture of a medicament for the treatment or prevention of tumor metastasis.

36.- Use of a compound of formula I according to any of claims 1 to 23 or a pharmaceutically acceptable salt, solvate or prodrug thereof for the manufacture of a medicament for the treatment or prevention of ischemia-reperfusion disorders.

37.- Use according to claim 36 wherein the ischemia-reperfusion disorder is selected from acute coronary diseases and stroke.